



### **AMENDMENTS TO THE CLAIMS:**

Please amend claims 6, 9, 32 and 45 as set forth below. The listing of claims will replace all prior versions, and listings of claims in the application:

### **LISTING OF THE CLAIMS**

1. (Cancelled)
2. (Cancelled)
3. (Cancelled)
4. (Withdrawn) An isolated protein encoded for by the nucleic acid sequence of SEQ ID NO: 1.
5. (Withdrawn) An isolated protein of claim 4 having the amino acid sequence of SEQ ID NO: 2.
6. (Currently Amended) A method for detecting the susceptibility to<sub>1</sub> or the presence of<sub>1</sub> existing basement membrane disease comprising the steps of providing a nucleic acid sample containing the NPHS1 gene<sub>1</sub> or<sub>7</sub> fragments thereof, from an individual; and detecting a mutation in said gene, or some fragment thereof, wherein if an individual is susceptible to<sub>1</sub> or ~~have~~ has the basement membrane disease<sub>1</sub> have the individual has at least one mutation in said gene.
7. (Cancelled)
8. (Cancelled)
9. (Currently Amended) A method as in claim 6, wherein said basement membrane disease is congenital ~~nephritic~~ nephrotic syndromes of the Finnish type.
10. (Cancelled)

11. (Withdrawn) A method for treating an individual with basement membrane disease comprising administering an effective therapeutic amount of a protein of claim 4.

12. (Withdrawn) A method for treating an individual with basement membrane disease comprising administering an effective therapeutic amount of nucleic acid constructs containing an expressible nucleic acid sequence of SEQ ID NO: 1.

13. (Withdrawn) A polyclonal antiserum containing antibodies specific for nephrin protein produced by immunizing an animal with a sufficient amount of the protein of claim 5 to stimulate an immune response.

14. (Withdrawn) A monoclonal antibody specific for nephrin produced by immunizing a rodent with a sufficient amount of the protein of claim 5 to stimulate an immune response.

15. (Withdrawn) A chimeric antibody comprising the variable domains of the antibody of claim 14 functionally attached to human antibody constant domains.

16. (Withdrawn) A kit for screening individuals for susceptibility to basement membrane disease, or the present of basement membrane disease, containing at least one antibody specific for nephrin.

17. (Withdrawn) A method for identifying a small molecule therapeutic for the treatment of proteinuria associated with kidney disease comprising screening candidate molecules for specific binding to the nephrin protein.

18. (Withdrawn) A method as in claim 17 wherein said specific binding effects a change in nephrin protein bioactivity.

19. (Previously Presented) A method for diagnosing the presence of a basement membrane disease in an individual, comprising detecting the presence of a mutation in exon 2 or exon 26 of the NPHS1 gene, wherein the mutation in at least one of the exons results in a premature stop codon in the exon.

20. (Previously Presented) The method of claim 19, wherein the NPHS1 gene comprises SEQ ID. NO: 1.

21. (Previously Presented) The method of claim 19, wherein the mutation in exon 2 comprises a two base pair deletion.

22. (Previously Presented) The method of claim 21, wherein the NPHS1 gene is amplified prior to detecting the presence of the mutation in exon 2.

23. (Previously Presented) The method of claim 22, wherein the amplification is by PCR and the primers used for amplification specifically amplify the exon 2 region of the NPHS1 gene.

24. (Previously Presented) The method of claim 23, wherein the primers used for amplification comprise DNA sequences comprising SEQ ID NO: 3 or SEQ ID NO: 4.

25. (Previously Presented) The method of claim 19, wherein the mutation in exon 26 comprises a single base change.

26. (Previously Presented) The mutation of claim 25, wherein the single base pair change results in the nonsense mutation CGA - >TGA.

27. (Previously Presented) The method of claim 25, wherein the NPHS1 gene is amplified prior to detecting the presence of the mutation in exon 26.

28. (Previously Presented) The method of claim 27, wherein the amplification is by PCR and the primers used for amplification specifically amplify the exon 26 region of the NPHS1 gene.

29. (Previously Presented) The method of claim 28, wherein the primers used for amplification comprise DNA sequences comprising SEQ ID NO: 5 or SEQ ID NO: 6.

30. (Previously Presented) The method of claim 29, wherein a novel restriction site is detected in the amplified product.

31. (Previously Presented) The method of claim 30, wherein the novel restriction site is susceptible to digestion with DdeI.

32. (Currently Amended) A method of determining whether an individual is at risk for developing a congenital ~~nephritic~~ nephrotic syndrome of the Finnish type NPHS1, comprising analyzing a nucleic acid sample containing the NPHS1 gene, wherein the method comprises analyzing the exon 2 or exon 26 region of the NPHS1 gene, wherein an individuals at risk for developing ~~NPHS1~~ have a congenital nephrotic syndrome has at least one a mutation in either or both ~~one or more~~ of the exons.

33. (Previously Presented) The method of claim 32, wherein the NPHS1 gene comprises SEQ ID NO: 1.

34. (Previously Presented) The method of claim 32, wherein the mutation in exon 2 comprises a two base pair deletion.

35. (Previously Presented) The method of claim 34, wherein the NPHS1 gene is amplified prior to detecting the presence of the mutation in exon 2.

36. (Previously Presented) The method of claim 35, wherein the amplification is by PCR and the primers used for amplification specifically amplify the exon 2 region of the NPHS1 gene.

37. (Previously Presented) The method of claim 36, wherein the primers used for amplification comprise DNA sequences selected from the group consisting of SEQ ID NOS: 3 and or SEQ ID NO: 4.

38. (Previously Presented) The method of claim 32, wherein the mutation in exon 26 comprises a single base pair change.

39. (Previously Presented) The mutation of claim 38, wherein the single base pair change results in the nonsense mutation CGA - >TGA.

40. (Previously Presented) The method of claim 39, wherein the NPHS1 gene (SEQ ID NO: 1) is amplified prior to detecting the presence of the mutation in exon 26.

41. (Previously Presented) The method of claim 40, wherein the amplification is by PCR and the primers used for amplification specifically amplify the exon 26 region of the NPHS1 gene.

42. (Previously Presented) The method of claim 41, wherein the primers used for amplification comprise DNA sequences selected from the group consisting of SEQ ID NOS: 5 and SEQ ID NO: 6.

43. (Previously Presented) The method of claim 42, wherein a novel restriction site is detected in the amplified product.

44. (Previously Presented) The method of claim 43, wherein the novel restriction site is susceptible to digestion with DdeI.

45. (Currently Amended) A method for determining that an individual is not at risk for developing congenital ~~nephritic~~ nephrotic syndrome of the Finnish Type NPHS1, wherein the NPHS1 is associated with a mutation in exon 2 or exon 26 of the NPHS1 syndrome gene, comprising analyzing a nucleic acid sample containing the NPHS1 syndrome gene, wherein the method comprises analyzing the exon 2 or exon 26 region of the NPHS1 gene, wherein the individual not at risk for developing NPHS1 the syndrome does not have a mutation in exon 2 or exon 26.

46. (Previously Presented) The method of claim 45, wherein the NPHS1 gene comprises SEQ ID NO: 1.

47. (Previously Presented) The method of claim 45, wherein the NPHS1 gene is amplified prior to analysis.

48. (Previously Presented) The method of claim 47, wherein the amplification is PCR amplification using primers comprising a DNA sequence selected from the group consisting of: SEQ ID NO: 3; SEQ ID NO: 4; SEQ ID NO: 5 and SEQ ID NO: 6.

49. (Previously Presented) A method for detecting the presence or absence of a mutation in the NPHS1 gene, comprising the steps of:

analyzing a nucleic acid test sample containing the NPHS1 gene for at least one mutation in exon 2 or exon 26 of the gene;

comparing the results of the analysis of the test sample of step a) with the results of the analysis of a control sample, wherein the control sample comprises a NPHS1 gene without a mutation in exon 2 or exon 26; and

determining the presence or absence of at least one mutation in exon 2 or exon 26 in the test sample.

50. (Previously Presented) The method of claim 49, wherein the NPHS1 gene comprises SEQ ID. NO: 1.

51. (Previously Presented) The method of claim 49, wherein the mutation in exon 2 is a two base pair deletion and the mutation in exon 26 is a single base pair change, wherein either mutation results in a premature stop codon in the exon.

52. (Previously Presented) The method of claim 49, wherein the NPHS1 gene is amplified prior to analysis.

53. (Previously Presented) The method of claim 52, wherein the amplification is PCR amplification using primers comprising a DNA sequence selected from the group consisting of: SEQ ID NO: 3; SEQ ID NO: 4; SEQ ID NO: 5 and SEQ ID NO: 6.

54. (Previously Presented) A primer comprising a nucleic acid sequence comprising SEQ ID NO: 3, SEQ ID NO: 4; SEQ ID NO: 5 or SEQ ID NO: 6.